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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,898	09/29/2006	Keiko Matsumoto	081356-0267	8308

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1657	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,898	MATSUMOTO ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/06/09; 12/28/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the Group I, claims 1-8, in the reply filed on 4/28/2009 is acknowledged.

Claims 9-13 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected invention(s), there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 4/28/2009.

Claims 1-8 are under examination in the instant office action.

Claim Objections

Claims 4-8 are objected to under 37 CFR 1.75(c) as being in improper form because they are presented as multiple dependent claims. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is recites "a single measurement" but it is unclear what is measured. There are at least two separate amounts including LDL cholesterol and total cholesterol as intended to be quantified, thus, there should be at least two measurements not a single measurement. The specification Figure 1 describes 2 measurements. The depending claim 5 recites measurements of "two values". The depending claim 8 recites different measurement conditions. Therefore, claim 1 is as being incomplete for omitting essential elements or essential structural cooperative

relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01.

Claim 1 also recites several manipulations and/or events during "second step" including first converting, second treating, second converting and "single measurement". Thus, the second step appears to include several active steps as intended. Therefore, claim 1 is being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Claim 1 is also rendered indefinite by the phrase "quinine dye is not formed" because it is uncertain what manipulations are intended for the claimed method. Is the quinine dye colorless? Is a portion of hydrogen peroxide and/or quinine dye selectively eliminated or manipulated or measured?

Claim 2 is indefinite and incomplete with regard to active/functional components in reagent compositions for each step. For example: peroxidase is included in all reagent compositions with 4-aminoantipyrine, phenolic and/or anilinic compounds. Thus, hydrogen peroxide would be decomposed during the "first step".

Claims 5-8 recite the limitation "two values", "change in absorbance" and "different measurement conditions" in the method requiring "a single measurement". There is insufficient antecedent basis for these limitations encompassing several measurements in the claim 1 limited to a single measurement. Claims 5-8 appear to extend rather than limit the claimed method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(a) as being anticipated by the reference by Hiroshi Matsui (IDS reference; Japanese Journal of Clinical Laboratory Automation, August 2003, 28(4), page 380).

Claims are directed to a method of quantification for cholesterol in low density lipoprotein (LDL) and total cholesterol in a biological sample wherein the method comprises a first step of treating lipoproteins other than LDL in the biological sample to generate hydrogen peroxide and a second step comprising sub steps of converting the hydrogen peroxide obtained in the first step to a quinone dye, treating remaining LDL and converting generated hydrogen peroxide to the quinone dye; wherein the quinone dye is not formed in the first step; and wherein cholesterol in LDL and total cholesterol are quantified from the amount of the quinone dye formed in the second step by "a single measurement".

Some claims are further directed to the use of reagent compositions comprising peroxidase and 4-aminoantipyrine, a phenolic or anilinic hydrogen donor compounds that are used either in the first step or in the second step. Some claims are further drawn to the use of cholesterol esterase and cholesterol oxidase and a surfactant that acts on lipoproteins other than LDL to generate hydrogen peroxide in the first step and the use of cholesterol esterase and cholesterol oxidase and a surfactant that acts on LDL to generate hydrogen peroxide in the second step. Some claims are further drawn to measuring changes in absorbance or at least "two values" as result of addition of the reagent mixtures, hydrogen peroxide generation and/or

formation of dyes that would reflect the amount of total cholesterol and the amount of cholesterol present in LDL. Some claims are further drawn to the use of automatic analyzer for clinical chemistry testing.

The cited reference by Hiroshi Matsui (August 2003) teaches a method of quantification for LDL cholesterol and total cholesterol in a biological sample by "a single measurement" wherein the difference in absorption change is measured as result of first step of treating lipoproteins other than LDL in the biological sample to generate hydrogen peroxide and as result of second step comprising sub-steps of converting the hydrogen peroxide obtained in the first step to a quinone dye, treating remaining LDL and converting generated hydrogen peroxide to the quinone dye. The reference clearly teaches measuring absorbance and, thus, the common reagents of the common cholesterol assays that usually include peroxidase, 4-aminoantipyrine, phenolic and/or anilinic compounds have been used in the method of the cited reference. Thus, the cited reference by Hiroshi Matsui (August 2003) is considered to anticipate the presently claimed invention.

Claims 1-8 rejected under 35 U.S.C. 102(b) as being anticipated by US 6,057,118 (Nakamura et al).

Claims as above.

US 6,057,118 (Nakamura et al) discloses a method of quantification for LDL cholesterol in low density lipoprotein (LDL) and total cholesterol in a biological sample wherein the method comprises first treating lipoproteins other than LDL in the biological sample to generate hydrogen peroxide while retarding reaction of LDL cholesterol and further measuring changes in

absorbance or at least "two values" as result of addition of the reagent mixtures, hydrogen peroxide generation and/or formation of dyes that would reflect the amount of total cholesterol (HDL, VLDL, etc.) and the amount of cholesterol present in LDL. US 6,057,118 (Nakamura et al) discloses that the reagent compositions comprise peroxidase and 4-aminoantipyrine, a phenolic or anilinic hydrogen donor compounds (see examples 1-2). Thus, the cited patent US 6,057,118 (Nakamura et al) is considered to anticipate the presently claimed invention.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Kanno et al. (IDS reference; Current Therapy, 1998, vol.16, No. 1, pages 146-150).

Claims as above.

The reference by Kanno et al. discloses a method of quantification for LDL cholesterol and total cholesterol in a biological sample wherein the method comprises first step of adding first reagent mixture for treating lipoproteins other than LDL in the biological sample to generate hydrogen peroxide from cholesterol of lipoproteins other than LDL and then second step of adding second reagent mixture for treating LDL cholesterol to generate hydrogen peroxide from LDL cholesterol. During first step the quinone dye is not formed and/or the reaction is colorless as result addition of first reaction mixture comprising peroxidase and 4-aminoantipyrine. During second step the color developing reagent that is not added in the first step (such as phenolic or anilinic hydrogen donor compounds) are added and the hydrogen peroxide generated from LDL cholesterol is subjected to color reaction and quantified by measuring changes in absorbance. Thus, the cited reference by Kanno et al. is considered to anticipate the presently claimed invention.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,925,534 (Miki et al.).

Claims as above.

US 5,925,534 (Miki et al.) discloses a method of quantification for LDL cholesterol and total cholesterol including HDL and VLDL in a biological sample wherein in the cited method the reaction with LDL begins after substantial completion of reactions with other than LDL such as HDL and VLDL (entire document including figures 2-13) as result of adding different reaction/reagent mixtures at different stages/steps. The color reaction is quantified by measuring changes in absorbance. The reaction/reagent mixtures comprise CHO and CO enzymes, surfactants that selectively act either on non-LDL or on LDL, peroxidase, 4-aminoantipyrine, phenolic or anilinic hydrogen donor compounds (reagent solutions 14-21 in the examples -5).

At the first stage during or after applying first reaction/reagent mixtures the quinone dye is not formed because the reaction is either colorless or because the generated hydrogen peroxide is eliminated. The reagent compositions not added in the first step are added at the second stage and these alternative reagents are either one of 4-aminoantipyrine or phenolic or anilinic hydrogen donor compound. For example: see reagent solutions 15 and 16 wherein "R-1" contains HDAOS (phenolic or anilinic hydrogen donor compound) and "R-2" contains 4-AA (4-aminoantipyrine).

Thus, the cited patent US 5,925,534 (Miki et al.) is considered to anticipate the presently claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hiroshi Matsui (IDS reference; Japanese Journal of Clinical Laboratory Automation, August 2003, 28(4), page 380), US 6,057,118 (Nakamura et al), Kanno et al. (IDS reference; Current Therapy, 1998, vol.16, No. 1, pages 146-150) and US 5,925,534 (Miki et al.).

Claims as above.

The cited references by Hiroshi Matsui, US 6,057,118 (Nakamura et al), Kanno et al. and US 5,925,534 (Miki et al.) are relied upon as explained above for the disclosure of methods of quantification for LDL cholesterol and total cholesterol in a biological sample wherein the method comprises first step of treating lipoproteins other than LDL in the biological sample to generate hydrogen peroxide and a second step comprising sub steps of converting the hydrogen peroxide obtained in the first step to a quinone dye, treating remaining LDL and converting generated hydrogen peroxide to the quinone dye. In the methods of the cited references the "quinone dye is not formed" during fist stage or first step because the cholesterol reaction is either delayed or it colorless or because generated hydrogen peroxide is eliminated. In the methods of the cited references the difference in absorbance is evaluated as "a single measurement" using automatic analyzers for clinical chemistry testing. In the methods of the cited references the reagent compositions comprise peroxidase and 4-aminoantipyrine, a

phenolic or anilinic hydrogen donor compounds that are used either in the first step or in the second step.

Thus, taken separately or as a whole the cited references teach and/or suggest the applicants' method within the broadest meaning of the instant claims. Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to practice the presently claimed method with a reasonable expectation of success in quantification of LDL cholesterol and total cholesterol in a biological sample. The claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

September 26, 2009

/Vera Afremova/

Primary Examiner, Art Unit 1657